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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,612	08/05/2005	Fritz H. Bach	15757-006US1	4076
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EXAMINER ROBINSON, HOPE A				
ART UNIT 1652		PAPER NUMBER		
NOTIFICATION DATE 04/20/2009		DELIVERY MODE ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

### Office Action Summary

**Application No.**

10/511,612

**Applicant(s)**

BACH ET AL.

**Examiner**

HOPE A. ROBINSON

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12/26/08.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 8-15, 19 and 20 is/are rejected.
- 7) ☒ Claim(s) 6, 7 and 16-18 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 October 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Application Status***

1. Applicant's response filed on December 26, 2008 is acknowledged.

### ***Claim Disposition***

2. Claims 1-20 are pending and are under examination.

### ***Maintained-Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1-5, 8-15 and 19-20 remain rejected under 35 U.S.C. 102(a) as being anticipated by Otterbein et al. (U.S. Patent No. 7,364,757, February 13, 2002).

Otterbein et al. teach that CO has potent anti-inflammatory effects and possibly suppresses intimal hyperplasia by inhibiting inflammation (see paragraph 182). In

addition, Otterbein et al. teach that (see paragraph 4) "Heme oxygenase-1 (HO-1) catalyzes the first step in the degradation of heme. HO-1 cleaves the .alpha.-meso carbon bridge of b-type heme molecules by oxidation to yield equimolar quantities of biliverdin IXa, carbon monoxide (CO), and free iron. Subsequently, biliverdin is converted to bilirubin via biliverdin reductase, and the free iron is sequestered into ferritin (the production of which is induced by the free iron)". The condition of intimal hyperplasia (thickening of Tunica intima of a blood vessel) is described in the reference as caused by transplantation or angioplasty (see paragraph 9).

Further, the reference discloses that HO-1 expression in a cell can be increased via gene transfer. As used herein, the term "express(ed)" means to cause increased production of a protein, e.g., HO-1 or ferritin in isolated cells or the cells of a tissue, organ or animal using an exogenously administered gene (e.g., a recombinant gene). The HO-1 or ferritin is preferably of the same species (e.g., human, mouse, rat, etc.) as the recipient, in order to minimize any immune reaction. Expression could be driven by a constitutive promoter (e.g., cytomegalovirus promoters) or a tissue-specific promoter (e.g., milk whey promoter for mammary cells or albumin promoter for liver cells). An appropriate gene therapy vector (e.g., retrovirus, adenovirus, adeno associated virus (AAV), pox (e.g., vaccinia) virus, human immunodeficiency virus (HIV), the minute virus of mice, hepatitis B virus, influenza virus, Herpes Simplex Virus-1, and lentivirus) encoding HO-1 or ferritin would be administered to the patient orally, by inhalation, or by injection at a location appropriate for treatment intimal hyperplasia. Similarly, plasmid

vectors encoding HO-1 or apo-ferritin can be administered, e.g., as naked DNA, in liposomes, or in microparticles" (see paragraph 117).

Otterbein et al. also teach at paragraph 119, that "alternatively or in addition, any of the products of metabolism by HO-1, e.g., bilirubin, biliverdin, iron, and/or ferritin can be administered to a patient in conjunction with, or instead of, carbon monoxide in order to prevent or treat intimal hyperplasia. Further, the present invention contemplates that iron-binding molecules other than ferritin e.g., desferoxamine (DFO), iron dextran, and/or apo-ferritin, can be administered to the patient. Further still, the present invention contemplates that enzymes (e.g., biliverdin reductase) that catalyze the breakdown any of these products can be inhibited to create/enhance the desired effect".

At paragraph 127 Otterbein et al. links the condition to atherosclerosis and describes the surgical procedure of balloon angioplasty (vascular surgery). Therefore, the limitations of the claims are met by the reference.

4. Claims 1-5, 8-15 and 19-20 remain rejected under 35 U.S.C. 102 (e) as being anticipated by Bach et al. (U.S. Patent No. 7,238,469, June 21, 2001).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in

the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Bach et al. teach Islet cell transplantation and complications with this process (i.e. non-specific inflammation). In addition, Bach et al. disclose that "unfettered EC activation, as during acute and chronic inflammation can lead to EC injury and apoptosis. Bach et al. disclose that EC apoptosis is a prominent feature associated with acute and/or chronic inflammation such as it occurs during hyperoxia, endotoxic shock, arteriosclerosis, ischemia reperfusion injury, and acute or chronic graft rejection (see paragraph 7).

Bach et al. disclose that HO-1 expression in a cell can be increased via gene transfer. Bach et al. state that as used herein, the term "express(ed)" means to cause increased production of a protein, e.g., HO-1 or ferritin in isolated cells or the cells of a tissue, organ or animal using an exogenously administered gene (e.g., a recombinant gene). Bach et al. also disclose that the HO-1 or ferritin is preferably of the same species (e.g., human, mouse, rat, etc.) as the transplant recipient, in order to minimize any immune reaction. The reference disclose that expression could be driven by a constitutive promoter (e.g., cytomegalovirus promoters) or a tissue-specific promoter (e.g., milk whey promoter for mammary cells or albumin promoter for liver cells). An appropriate gene therapy vector (e.g., retrovirus, adenovirus, adeno associated virus (AAV), pox (e.g., vaccinia) virus, human immunodeficiency virus (HIV), the minute virus of mice, hepatitis B virus, influenza virus, Herpes Simplex Virus-1, and lentivirus) encoding HO-1 or ferritin would be administered to the patient orally, by inhalation, or by

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injection at a location appropriate for treatment of transplant rejection (see paragraphs 115-117).

In addition, it is disclosed that, particularly preferred is local administration directly to the donor's organ, tissue or cells to be transplanted, or to the site of the transplant in the recipient. Similarly, plasmid vectors encoding HO-1 or apo-ferritin can be administered, e.g., as naked DNA, in liposomes, or in microparticles. Bach et al. teaches that any of the products of metabolism by HO-1, e.g., bilirubin, biliverdin, iron, and/or ferritin can be administered to a patient in conjunction with, or instead of, carbon monoxide in order to prevent or treat the disorder (see paragraph 117).

Further, Bach et al. teach iron-binding molecules other than ferritin e.g., desferoxamine (DFO), iron dextran, and/or apoferritin, can be administered to the patient. Any of the above compounds can be administered to the patient topically and/or systemically.

Bach et al. also teach that the administration of nitric oxide (NO) to a patient, organ(s), tissue(s) and/or isolated cells in conjunction with administration of carbon monoxide, HO-1 and/or HO-1 associated compounds. This technique includes providing NO to the donor, the recipient, or the organ, tissue or cell ex vivo, in conjunction with the administration of HO-1 and/or any or all of the products of heme degradation, e.g., CO, biliverdin, bilirubin, iron, and ferritin (see paragraph 118). Therefore, the limitations of the claims are met by the reference.

***Response to Arguments***

5. Applicant comments have been considered in full. Note that the art rejections of record remains. Applicant state that the claimed invention has been amended to be directed to particular inflammatory disorders, however, the Otterbien et al. reference remains relevant as the reference discloses that CO has potent anti-inflammatory effects and teaches HO-1 expression with enhancements. Applicant states that the "examiner is of the opinion that", however, the teachings of the reference is cited in the rejections not the examiner's opinions.

With regard to the rejection over Bach et al. applicant state that the claims are amended to directly claim inflammatory diseases, however, Bach et al. teach inflammatory disorders (i.e. acute and chronic inflammation). Therefore, the arguments presented are not persuasive and the rejection remains.

***Conclusion***

6. No claims are allowable as claims 6-7 and 16-18 are objected to as depending from a rejected based claim.

7. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to HOPE A. ROBINSON whose telephone number is (571)272-0957. The examiner can normally be reached on Monday-Friday 9:00-6:30 from 9:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed, can be reached at (571) 272-0934.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Hope A. Robinson/

Primary Examiner, Art Unit 1652